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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,606	11/13/2006	Robert L. Fine	68074-A-PCT-US/JPW/CH	4899

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
10/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,606	FINE ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,9-18,31,36,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-6, 9-18, 31, 36, 41-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/29/2009* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment and Arguments

The Amendment filed on 8/21/2008 in response to the previous Non-Final Office Action (2/22/2008) is acknowledged and has been entered.

Claims 41-42 are added.

Claims 2, 7-8, 19-30, 32-33, 37-40 are cancelled.

Claims 1, 3-6, 9-18,31, 36, and 41-42 are pending and the claims, drawn to a polypeptide of SEQ ID NO: 3 (linked SEQ ID NO: 1 and 2 as dimers or a tetramer) and a method of treating cancer with the peptide of claim 1, are examined on the merits.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 6/29/2009 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Rejection Maintained and Response to Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1, 3, 9-10, 14, 15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al (PNAS vol 92, page 9455-9459, 1995) in view of Hoffman

et al (US Patent No 5545727, issues 1996) as evidenced by sequence search result for the reasons below:

Amended claims recite a peptide comprising (having) the amino acids of SEQ ID NO: 3 or SEQ ID NO: 5.

SEQ ID NO: 3 is the originally claimed sequences of SEQ ID NO: 1 and 2 linked at 3' ends as 3'C-C3' by glycine.

SEQ ID NO: 1 has the aa 353-393 of p53 protein. SEQ ID NO: 2 is the palindrome of SEQ ID NO: 1.

SEQ ID NO: 5 is a dimer of SEQ ID NO: 3 or a tetramer of SEQ ID NO: 1 or 2.

SEQ ID NO: 3 has the following structure:

5' 353___393 3'-(Gly)-3' 393_____353 5' (393-353 is amino acid position of p53)

The Gly may be present or absent.

SEQ ID NO: 5 is a dimer of SEQ ID NO: 3

5' 353_____393 3'-(Gly)-3' 393_____353 5'-5' 353____393 3'-(Gly)-3'393____353 5'

Reed et al teach the dimer or tetramer of the fragments (aa 318-393) of p53 having the following structure:

5' 318___353___393 3' : 3' 393___353___318 5'.

It is clear that the fragment 318-393 of p53 comprises the fragment of 353-393 of p53, thus, the dimer or tetramer of the fragments would comprises the SEQ ID NO: 3 (dimer) or SEQ ID NO: 5 (tetramer) as shown in diagram above.

Applicant agrees the dimer or tetramer of the p53 fragments comprising the SEQ ID NO: 3 or 5, but, argues that Reed's dimer or tetramer is non-covalently associated peptide and there is no teaching or suggesting the amino acids 353-393 of p53 linking to 393-353 of p53 (page 7-8). This has been considered, but not persuasive for the following reasons: Reed et al explicitly teach that p53 binding to a DNA for performing the function requiring a mirrored dimer or tetramer structure of the p53 fragment. Reed et al specifically teach the c-terminal aa 360-393 of p53 is the basic structure for p53 binding to the DNA (fig 4, page 9459). Such teaching strongly suggests one skilled in the art to take the fragments of the p53 protein to covalently link them together for the purpose of medical or therapeutic use. One skilled in the art would be motivated to do so with expectation of success based on the teaching of Hoffman et al on how to make a fusion protein or multimer with or without glycine.

Applicant further agues that the reference of Reed et al do not teach:

(a) deleting a stretch of amino acids from the 318-393 amino acid portion of human p53 disclosed in Reed.
(b) joining four of such truncated stretches together as a single polypeptide,
(c) reversing the order of a repeat.

In response, the claims reciting the amino acids comprising the dimer or tetramer of the sequence of SEQ ID NO: 1 (aa 353-393 of p53). Thus, the peptide of Reed is within the scope of claimed invention. Reed et al although do not disclose joining the peptide as a single polypeptide, Reed et al do suggest the mirror structure of the peptide as dimer or tetramer for function. If the structure is mirrored peptides, it would be reversing the order of a repeat (again see figure 4).

Applicant further argues that Reed teaches p53 tetramer of 318-393 while the instant claims recite only amino acids 353-393 (page 9). In response, instant claims reciting the amino acid having ...., word having is the same meaning as "comprising", which allows one or more amino acids added to one or two ends of sequence of 353-393, such as to 318-393. In addition, Reed did suggest the basic structure having aa 360-393 of p53 as stated above.

Applicant further argues that Hoffman teaches three types of linkers, triple glycines, a glycine and a proline, the examiner gives not reason why to only choose single glycine, not three glycines or not single proline as a linker (page 9, line paragraph). In response, as set forth in the rejection and cited section, Hoffman clearly states that glycine is the preferred amino acid in the linkers because it is quite flexible. Hoffman also teaches an example of forming a dimer with single glycine (example 26, col 84, line 14). In addition, one skilled in the art would also have a choice to use any of the linkers and preferred glycine as suggested by Hoffman et al (see the same section in the rejection, col 34, line 54-56 in particular).

2. Claims 1, 4-6, 9, 11-14, 16-18, 31 and 36 remain and claims 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al., (PNAS vol 92, page 9455-9459, 1995) in view of Hoffman et al., (US Patent No 5545727, issues 1996) as evidence by sequence search result as applied to claims 1, 7-9, and 14 above, and further in view of Pincus, M. WO2003/105880, filing March 2003, priority to March 2002, Published Dec. 2003).

Application provides the same arguments as above regarding the teaching of Reed and Hoffman (page 12-13). The arguments have been responded above. Applicant does not provide detailed argument for the teaching of Pincus et al except stating adding the penetrating sequence of Pincus would not result in or render obvious applicant's different claimed sequence.

Applicant provides exhibit 1, an article by LaFevre-Bernt et al who teach that " it is well known that the p53 protein tetramized through a non-covalent dimer model naturally" (bridging page 11-12). In response, the teaching of LaFevre-Bernt et actually support the Office's position, that is, the fragments of p53 form a tetramer for function naturally. Applicant is claiming a non-natural peptide and using the natural function for the purpose of therapeutic use. Thus, taking the suggestion of Reed and/pr the teaching of LaFevre-Bernt et al, one skilled in the art would consider forming such dimer or tetramer by covalently linking them together in order to let the dimer to tetramer more stable and flexible during the treatment in vivo or even in vitro.

Claim 31 is direct to a method of treating a cancer with the peptide of claim 1. Applicant, on page 14, argues since claim 1 is not obvious, the subject matter of claim 31 is not obvious also since the arts do not disclose or suggest repeating p53 fragment for treating a cancer. In response, claim 1 being obvious over the reference alone (Reed) or in combination has been discussed above. Pincus did teach a method of making a pharmaceutical composition for treating a cancer comprising using a p53 fragment. It would be obvious to replace the fragment of p53 in the method of Pincus with the fragment repeat(s) disclosed by Reed for treating a cancer with expected result.

One skill in the art would be motivated with expectation of success to treat a patient with the material because Reed suggests that p53 must form a dimer or tetramer to perform a function as a tumor suppressor. Thus, Applicant's argument has not been found persuasive, and the rejection is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao/
Examiner, Art Unit 1642

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643